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(54) Title: TARGETED WHOLE GENOME AMPLIFICATION METHOD FOR IDENTIFICATION OF PATHOGENS

(57) Abstract: The methods disclosed herein relate to methods and compositions for amplifying nucleic acid sequences, more specifically, from nucleic acid sequences of pathogens by targeted whole genome amplification.

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INTERNATIONAL SEARCH REPORT

International application No.
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A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C12P 19/34 (2008.04)
USPC - 435/91.2
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8)- C12P 19/34 (2008.04)
USPC- 435/91.2, 6; 702/19

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWEST(PGPB,USPT,USOC,EPAB,JPAB); Google Patents; Google Scholar
Isis, whole genome amplification, mass spectometry, patogen detection, sampath, hall, ecker, hofstadler, selective , targeted, discriminat$, specific, primer, phi29 high processivity polymerase. recombinant

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	TALAAT et al. Genome-directed primers for selective labeling of bacterial transcripts for DNA microarray analysis NATURE BIOTECHNOLOGY VOL 17 pg 679-682 JUNE 2000. (pg 679 para 2)(pg 680 Fig 1.)(pg 680 para 4)(pg 681 para 1-3)	1-41, 49-89
Y	US 2004/0126764 A1 (LASKEN et al.) 01 July 2004 (01.07.2004) (paras [0007][0010],[0017], [0039], [0040], [0048], [0051], [0103])	1-41, 49-89
Y	WO 2005/098047 A2 (SAMPATH et al.) 20 October 2005 (20.10.2005)(SEQ ID NOs:262,625,350,782,241,597,389)(para [0006]-[0009])(para [0012]-[0013])(para [0074-0075])	2-13, 19-31, 35, 36 52-63, 68-80, 82, and 84-89
Y	US 5,576,204 A (BLANCO et al.) 19 November 1996 (19.11.1996)(col 2 ln 18-30)(col 3 ln 12-18)(col 4 ln 21-25)	15, 16, 64-66
Y	WO 2005/054454 A1 (RAOULT et al) 16 June 2005 (16.06.2005) (SEQ ID NO:53) (SEQ ID NO:3 nucleotides 414-437)(abstract)	11,13, 61, 63
Y	US 2004/00291129 A1 (WANG et al.) 12 February 2004 (12.02.2004)(SEQ ID NOs:6545, 38904)(para [1785]-[1788])	11,12, 61, 62
Y	US 2003/0119018 A1 (OMURA et al.) 26 June 2003 (26.06.2003)(SEQ ID NO:4898 nucleotides 3299-3271)(para[0008]-[0010])	12, 62
Y	US 2005/0266397 A1 (ECKER et al.) 01 December 2005 (01.12.2005)(para [0015]-[0016])(para [0032])(para [0108])(para [0109])(para [0116-0117])(para [0118])	37-41 85-89

☒ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
20 November 2008 (20.11.2008)	08 JAN 2009
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (April 2007)

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	NEWCOMBE et al. PCR of Peripheral Blood for Diagnosis of Meningococcal Disease JOURNAL OF CLINICAL MICROBIOLOGY, July 1996, Vol. 34, No. 7 p. 1637-1640. (pg 1637-1638, materials and methods para 3)(pg 1639 para 2-3)	20-23, 69-72

INTERNATIONAL SEARCH REPORT

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

This application contains the following inventions or groups of inventions which are not so linked as to from a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1: Claims 1-41 and 49-89 are directed to a method comprising amplifying a genome with a plurality of whole genome amplification primers which are selected by a series of genome-evaluating steps, wherein claims 10 and 60 are limited to primer pair 346

Group 2: Claims 1-41 and 49-89 are directed to a method comprising amplifying a genome with a plurality of whole genome amplification primers which are selected by a series of genome-evaluating steps, wherein claims 10 and 60 are limited to primer pair 348

Group 3: Claims 1-41 and 49-89 are directed to a method comprising amplifying a genome with a plurality of whole genome amplification primers which are selected by a series of genome-evaluating steps, wherein claims 10 and 60 are limited to primer pair 349

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1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-41 and 49-89 wherein claims 10 and 60 are limited to primer pair 346

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

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Continuation of Box No. III Lack of Unity:

Group 4: Claims 1-10, 13-41, 49-60, and 63-89 are directed to a method comprising amplifying a genome with a plurality of whole genome amplification primers which are selected by a series of genome-evaluating steps, wherein claims 10, 13, 60, and 63 are limited to primer pair 354

Group 5: Claims 1-10, 13-41, 49-60, and 63-89 are directed to a method comprising amplifying a genome with a plurality of whole genome amplification primers which are selected by a series of genome-evaluating steps, wherein claims 10, 13, 60, and 63 are limited to primer pair 358

Group 6: Claims 1-10, 13-41, 49-60, and 63-89 are directed to a method comprising amplifying a genome with a plurality of whole genome amplification primers which are selected by a series of genome-evaluating steps, wherein claims 10, 13, 60, and 63 are limited to primer pair 359.

Group 7: Claims 1-11, 13-41, 49-61, and 63-89 are directed to a method comprising amplifying a genome with a plurality of whole genome amplification primers which are selected by a series of genome-evaluating steps, wherein claims 10, 13, 60, and 63 are limited to primer pair 3346

Group 8: Claims 1-10, 13-41, 49-60, and 63-89 are directed to a method comprising amplifying a genome with a plurality of whole genome amplification primers which are selected by a series of genome-evaluating steps, wherein claims 10, 13, 60, and 63 are limited to primer pair 449

Group 9: Claims 1-10, 13-41, 49-60, and 63-89 are directed to a method comprising amplifying a genome with a plurality of whole genome amplification primers which are selected by a series of genome-evaluating steps, wherein claims 10, 13, 60, and 63 are limited to primer pair 3350

Group 10: Claims 1-10, 14-41, 49-60, and 64-89 are directed to a method comprising amplifying a genome with a plurality of whole genome amplification primers which are selected by a series of genome-evaluating steps, wherein claims 10 and 60 are limited to primer pair 2249

Group 11: Claims 1-10, 12-41, 49-60, and 62-89 are directed to a method comprising amplifying a genome with a plurality of whole genome amplification primers which are selected by a series of genome-evaluating steps, wherein claims 10, 13, 60, and 63 are limited to primer pair 3361

Group 12: Claims 1-10, 13-41, 49-60, and 63-89 are directed to a method comprising amplifying a genome with a plurality of whole genome amplification primers which are selected by a series of genome-evaluating steps, wherein claims 10, 13, 60, and 63 are limited to primer pair 3360

Group 13: Claims 42-48, and 89 are directed to a diagnostic kit comprising a high processivity polymerase enzyme and a plurality of purified targeted whole genome amplification primers, wherein claims 44 is limited to primer pair 346

Group 14: Claims 42-48, and 89 are directed to a diagnostic kit comprising a high processivity polymerase enzyme and a plurality of purified targeted whole genome amplification primers, wherein claims 44 is limited to primer pair 348

Group 15: Claims 42-48, and 89 are directed to a diagnostic kit comprising a high processivity polymerase enzyme and a plurality of purified targeted whole genome amplification primers, wherein claims 44 is limited to primer pair 349

Group 16: Claims 42-44, 47, 48, and 89 are directed to a diagnostic kit comprising a high processivity polymerase enzyme and a plurality of purified targeted whole genome amplification primers, wherein claims 44 and 47 are limited to primer pair 354

Group 17: Claims 42-44, 47, 48, and 89 are directed to a diagnostic kit comprising a high processivity polymerase enzyme and a plurality of purified targeted whole genome amplification primers, wherein claims 44 and 47 are limited to primer pair 358

Group 18: Claims 42-44, 47, 48, and 89 are directed to a diagnostic kit comprising a high processivity polymerase enzyme and a plurality of purified targeted whole genome amplification primers, wherein claims 44 and 47 are limited to primer pair 359

Group 19: Claims 42-45, 47, 48, and 89 are directed to a diagnostic kit comprising a high processivity polymerase enzyme and a plurality of purified targeted whole genome amplification primers, wherein claims 44 and 47 are limited to primer pair 3346.

Group 20: Claims 42-44, 47, 48, and 89 are directed to a diagnostic kit comprising a high processivity polymerase enzyme and a plurality of purified targeted whole genome amplification primers, wherein claims 44 and 47 are limited to primer pair 449

Group 21: Claims 42-44, 47, 48, and 89 are directed to a diagnostic kit comprising a high processivity polymerase enzyme and a plurality of purified targeted whole genome amplification primers, wherein claims 44 and 47 are limited to primer pair 3350

Group 22: Claims 42-44, 48, and 89 are directed to a diagnostic kit comprising a high processivity polymerase enzyme and a plurality of purified targeted whole genome amplification primers, wherein claims 44 is limited to primer pair 2249

Group 23: Claims 42-44, 46-48, and 89 are directed to a diagnostic kit comprising a high processivity polymerase enzyme and a plurality of purified targeted whole genome amplification primers, wherein claims 44 and 47 are limited to primer pair 3361

Group 24: Claims 42-44, 47, 48, and 89 are directed to a diagnostic kit comprising a high processivity polymerase enzyme and a plurality of purified targeted whole genome amplification primers, wherein claims 44 and 47 are limited to primer pair 3360.

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Second Continuation Page of Box No. III. Lack of Unity:

The inventions listed as Groups I- XXIV do not relate to a single general inventive concept under PCT Rule 13.1 because under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of Groups I-XII is the series of genome-evaluating steps used to select primers, which is not present in Group XIII-XXIV that has a special technical feature of a high processivity polymerase enzyme.

The common technical feature of the listed groups is a whole genome primer. However, this is not an improvement over the prior art of US 2005/0037393 A1 to Gunderson et al. (17 Feb 2005) that teaches a whole genome amplification primer (para [0001]).

Additionally, a restriction is applied within Groups I-XII and Group XIII-XXIV because they relate to different primer pairs of distinct sequences having unrelated structures.